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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,632	HABERMANN, PAUL	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *3-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 7-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/13/02; 11/07/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-20 are pending in the application.

Election/Restriction

[2] Applicants' election with traverse of the invention of Group I and the species of mini-proinsulin, filed March 23, 2004 is acknowledged. Applicants assert that claims 1-2 and 7-20 read on the elected species.

Applicants traverse the restriction requirement by arguing that there is no serious burden to co-examine all pending claims. Applicants' argument is not found persuasive.

As stated in a previous Office action, MPEP § 803 states that a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search. First, it is noted that the inventions of Groups I and II have separate classification. Second, even assuming arguendo the inventions of Groups I and II had the same classification, it is noted that, while publications disclosing polynucleotide sequences typically disclose the corresponding polypeptide sequences, it is false to assume the only source of disclosure of a polypeptide is one in which the polynucleotide sequence is disclosed. Thus, as a separate search is required for the invention of Group I and the invention of Group II, co-examination of the claims of the inventions of Groups I and II would require a serious burden

Applicants traverse the election of species requirement by arguing that four species of proteins is not an unreasonable number of species. Applicants' argument is not found persuasive.

37 CFR § 1.141 states that "more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed species" (underline added for emphasis). In this case, claim 1, which is generic to the species recited in claims 2-3, is not allowable. As the proteins recited in claims 2-3 are distinct, the election of species requirement is proper in accordance with MPEP 806.04(a).

[3] The requirement is still deemed proper and is therefore made FINAL.

[4] Claims 3-6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

[5] Claims 1-2 and 7-20 are being examined on the merits.

Information Disclosure Statement

[6] All references cited in the information disclosure statements (IDSs) filed September 13, 2002 and November 07, 2002, with the exception of DE 10033195 A1 and DE 3430556 A1, have been considered by the examiner and a copy of each IDS is attached to the instant Office action. References DE 10033195 A1 and DE 3430556 A1 have not been considered as these references are not present in the instant application.

Specification/Informalities

[7] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Nucleic Acids Encoding Hirudin Fusion Proteins and Methods for Producing Hirudin Fusion Proteins".

[8] The use of the trademarks "Leukine®", "Refludan®", Calbiochem®", "Expedite™", "EasySelect™", and "Invitrogen®" has been noted in this application. The trademarks cited above and all others used in the specification should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[9] Claim(s) 1-2 and 7-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claim 1 (claims 2 and 7-20 dependent therefrom) is indefinite in the recitation of "a natural hirudin isoform". While it is acknowledged that the specification discloses two examples of natural hirudin isoforms (page 10, line 1 of the specification), it is unclear as to which hirudin isoform amino acid sequences are meant to be included as reference sequences and which are meant to be excluded. It thus follows that the scope of hirudin derivatives that are meant to be encompassed by the claim and which are meant to be excluded is unclear. It is suggested that applicants clarify the meaning of "a natural hirudin isoform" by, for example, identifying "a natural hirudin isoform" by a sequence identifier.

[b] Claim 16 is confusing in that it is unclear where the step of separating the fermentation supernatant from the host cell is to occur. In the interest of advancing prosecution, the examiner has interpreted the claim as meaning the fermentation supernatant is separated from the host cell prior to adjusting the pH of the supernatant. It is suggested that applicants clarify the meaning of the claim.

[c] Claim 17 is unclear in the recitation of "removing the protein encoded by protein(Y) from the fusion protein." Is the term meant to be interpreted as cleaving the protein encoded by protein(Y) from the fusion protein or is it meant to imply that the protein encoded by protein(Y) is purified from a mixture of the protein encoded by protein(Y) and the fusion protein? It is suggested that applicants clarify the meaning of the claim.

[d] Claim 20 is incomplete as the claim is drawn to a process for preparing insulin, however, the process of claim 14, from which claim 20 is dependent therefrom, is not

limited to a process for production of insulin. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[10] Claim(s) 1-2 and 7-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 (claims 7-20 dependent therefrom) and 2 are drawn to a genus of nucleic acid sequences as encompassed by the claims. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus.

Thus, when there is substantial variation within the genus, as is the instant case, one must describe a sufficient variety of species to reflect the variation within the genus. The specification discloses only three species of the genus of claimed nucleic acid sequences, i.e., the nucleic acid sequences obtained in Examples 1-3 of the instant specification (see pages 15-22 of the instant specification). While it is noted that the specification describes the structures of additional representative species of signal sequences (represented by Sx in claim 1) at page 28, the specification fails to describe any additional representative species of the claimed genus of nucleic acid sequences, which encompasses species that are widely variant in structure. As such, the disclosure of the three representative species of nucleic acid sequences is insufficient to be representative of the attributes and features of all species encompassed by the recited genus of nucleic acid sequences. Given the lack of description of a representative number of nucleic acid sequences, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[11] Claims 1-2 and 7-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid sequences prepared as described in Examples 1-3 of the specification and optionally having the signal sequences as set forth at page 28 of the specification, does not reasonably provide enablement for the broad scope of claimed nucleic acid sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: Claims 1 (claims 7-20 dependent therefrom) and 2 are so broad as to encompass a vast number of nucleic acid sequences comprising any promoter sequence, any signal or leader sequence, any nucleic acid encoding for hirudin or any hirudin derivative that is 40% homologous (interpreted as meaning 40% identical) to a natural hirudin isoform, any protein-encoding sequence, optionally a mini-proinsulin-encoding nucleic acid sequence or any derivative thereof, and any untranslated expression-enhancing nucleic acid. The broad scope of claimed nucleic acid sequences is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of promoters,

signal or leader sequences, hirudin or hirudin-derivative encoding nucleic acids, protein encoding nucleic acids, and untranslated expression enhancing sequences. In this case the disclosure is limited to those nucleic acid sequences prepared as described in Examples 1-3 of the specification and optionally having the signal sequences as set forth at page 28 of the specification.

- The lack of guidance and working examples: The specification provides only three working examples of the claimed nucleic acid sequences, i.e., those three nucleic acid sequences prepared as described in Examples 1-3 of the specification. The specification provides further guidance for additional signal sequences that may be used to substitute the signal sequence in the nucleic acid sequences constructed according to Examples 1-3 in the specification (see page 28 of the specification). However, these working examples and guidance regarding additional signal sequences fail to provide the necessary guidance for making the entire scope of claimed nucleic acid sequences.

- The high level of unpredictability in the art: The amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within an encoding nucleic acid's sequence where modifications can be made with a reasonable expectation of success

in obtaining an encoded polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. In this case, the necessary guidance has not been provided in the specification as explained above. Thus, a skilled artisan would recognize the high degree of unpredictability that the entire scope of nucleic acid sequences, including those encoding hirudin derivatives and mini-proinsulin derivatives, would encode a polypeptide having the desired anticoagulant and insulin activities.

- The state of the prior art supports the high level of unpredictability: The state of the art provides evidence for the high degree of unpredictability in altering a protein sequence with an expectation that the protein will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). While it is acknowledged that this reference was published in 1991, to date there remains no certain method for reasonably predicting the effects of even a *single* amino acid mutation on a protein.

- The amount of experimentation required is undue: While methods of generating variants of a given protein, e.g., site-directed mutagenesis, are known, it is not routine in the art to screen for all proteins having a substantial number of modifications having any function, as encompassed by the instant claims. Therefore, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[12] Claim(s) 1, 7-14, and 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Dawson et al. (US Patent 5,434,073). The claims are drawn to a nucleic acid sequence as set forth in claim 1, optionally wherein Y is a mini-proinsulin derivative, a vector or plasmid comprising said nucleic acid sequence, a host cell comprising said vector or plasmid, and methods for the production of a fusion protein.

Dawson et al. generally teach nucleic acids encoding hirudin fusion proteins. For example, Dawson et al. teach an expression vector encoding a hirudin-hirudin fusion protein comprising a galactose regulated promoter, a nucleotide sequence encoding an alpha-factor pro-peptide, a linker of Ser-Leu-Asp-Lys-Arg, an N-terminal hirudin, a Ile-Glu-Gly-Arg linker, a C-terminal hirudin or a C-terminal streptokinase, and a yeast PGK terminator (See Example 1, columns 11-13 and Examples 8-9, columns 25-27). Dawson et al. teach expression of the hirudin-hirudin or hirudin-streptokinase fusion proteins by culturing Saccharomyces cerevisiae transformed with the expression vector, followed by isolation of the fusion protein (Example 2, columns 13-14 and Example 15, column 32). This anticipates claims 1, 7-14, and 18-19 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

> matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[13] Claim(s) 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dawson et al. in view of Badziong et al. (US Patent 5,095,092). Claims 15-16 limit the method of claim 14.

Dawson et al. disclose the teachings as described above. The method of fusion protein purification of Dawson et al. does not comprise the steps as set forth in claims 15 and 17.

Badziong et al. teach a method of purifying hirudin by adjusting the pH of S. cerevisiae culture filtrate to a pH of between 2 and 8, applying the pH-adjusted filtrate to a chromatography resin followed by eluting the hirudin from the resin (column 2). Badziong et al. teach that this method has advantages over other methods of purifying hirudin from yeast culture supernatants (column 1).

Also, at the time of the invention, it was well-known in the art to remove the culture medium from an expression host that secretes a desired protein into the culture medium and to replace the medium with fresh medium for long-term continuous culture of the host cells to maximize production of the secreted protein.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Dawson et al. and Badziong et al. to separate the culture supernatant from the S. cerevisiae host cell, add fresh medium to the host cells for continued culturing, and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. One would have been motivated

separate the culture supernatant from the S. cerevisiae host cell, add fresh medium to the host cells for continued culturing, and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. in order to maximize production of the fusion protein using a single batch of culture and because of the advantages of using the method of Badziong et al. for purifying hirudin from yeast culture supernatant as described by Badziong et al. One would have a reasonable expectation of success for separating the culture supernatant from the S. cerevisiae host cell, adding fresh medium to the host cells for continued culturing, and to purify the fusion proteins of Dawson et al. from the supernatant using the method of Badziong et al. because of the results of Dawson et al. and Badziong et al. Therefore, claims 15-16, drawn to a method for producing hirudin, would have been obvious to one of ordinary skill in the art.

[14] Claim(s) 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dawson et al. in view of Bischoff et al. (J Chromatogr 476:245-255). Claim 17 limits the method of claim 14.

Dawson et al. disclose the teachings as described above. Dawson et al. additionally teach that following cleavage of the hirudin-hirudin fusion protein, the products of the cleavage reaction were analyzed by HPLC (Example 13, column 15). The method of fusion protein purification of Dawson et al. does not comprise a step of precipitating the fusion protein from the fermentation broth and further comprising cleaving the fusion protein and concentrating the protein by a chromatographic step.

Bischoff et al. teach a method for purifying recombinantly expressed and secreted hirudin from the culture medium of S. cerevisiae. The method involves filtering the supernatant, HPLC chromatography, precipitation with acetone, followed by HPLC (page 247).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Dawson et al. and Bischoff et al. to separate the culture supernatant from the S. cerevisiae host cell according to Bischoff et al., cleave the fusion protein, and analyze the components of the fusion protein by HPLC. One would have been motivated to separate the culture supernatant from the S. cerevisiae host cell according to Bischoff et al. in order to obtain highly purified hirudin. One would have a reasonable expectation of success for separating the culture supernatant from the S. cerevisiae host cell according to Bischoff et al., cleaving the fusion protein, and analyzing the components of the fusion protein by HPLC because of the results of Dawson et al. and Bischoff et al. Therefore, claim 17, drawn to a method for producing hirudin, would have been obvious to one of ordinary skill in the art.

Claim Rejections – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[15] Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 4 of US non-provisional application 10/076,634 ('634 Application). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 1 of the instant application is drawn to a nucleic acid sequence having the formula as set forth in the claim. Claim 4 of the '634 Application is drawn to a nucleic acid sequence having the formula as set forth in the claim. The claims differ in that the elements of the formula vary between the two claims and the protein(Y) of claim 1 of the instant application is limited to a nucleic acid encoding a protein that is produced and secreted by yeast (although the protein itself is not limited to being produced and secreted in yeast). The portion of the specification of the '634 Application that supports the claimed nucleic acid includes two embodiments of claim 4, i.e., a nucleic acid encoding a Ser-hirudin-GNSAR-simian proinsulin fusion protein (pages 18-20) and an Ala-hirudin-R-simian

proinsulin fusion protein (pages 20-22). Claim 1 of the instant application cannot be considered to be patentably distinct over claim 4 of the '634 Application when there is a specifically recited embodiment in the '634 Application that would anticipate claim 1. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

[16] Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of US non-provisional application 10/076,631 ('631 Application). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 1 of the instant application is drawn to a nucleic acid sequence having the formula as set forth in the claim. Claim 2 of the '631 Application is drawn to a nucleic acid sequence having the formula as set forth in the claim. The claims differ in that the elements of the formula vary between the two claims. The portion of the specification of the '631 Application that supports the claimed nucleic acid includes at least one embodiment of claim 2, i.e., a nucleic acid encoding a hirudin-mini-proinsulin fusion protein (pages 14-17). Claim 1 of the instant application cannot be considered to be patentably distinct over claim 2 of the

'631 Application when there is a specifically recited embodiment in the '631Application that would anticipate claim 1. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

[17] Status of the claims:

- Claims 1-20 are pending.
- Claims 3-6 are withdrawn from consideration.
- Claims 1-2 and 7-20 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652
05-13-04